RESPONSE UNDER 37 CFR 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP 1804

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No.:	**PENN-0065**
Inventors:	**Wolfe and Fraser**
Serial No.:	**08/393,066**
Filing Date:	**February 23, 1995**
Examiner:	**D. Crouch**
Group Art Unit:	**1804**
Title:	**Method of Delivering Genes to the Central Nervous System of a Mammal**

I, **Jane Massey Licata**, Registration No. **32,257**, certify that this correspondence is being deposited with the U.S. Postal Service as First Class mail in an envelope addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231.

On this date: **September 18, 1997**

Jane Massey Licata

Jane Massey Licata, Registration No. **32,257**

BOX AF
Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Dear Sir:

TRANSMITTAL LETTER

Transmitted herewith is an Reply Brief with Appendices One and Two, in triplicate, and Change of Attorney or Agent's Address in Application (37 C.F.R. 1.8(a)).

(XX) The Commissioner is hereby authorized to charge payment of the following fees associated with this communication or credit any overpayment to Deposit Account No. 12-1086. This sheet is attached in triplicate.

(XX) Any additional filing fees required under 37 CFR 1.16 including fees for presentation of extra claims.

(XX) Any additional patent application processing fees under 37 CFR 1.17 and under 37 CFR 1.20(d).

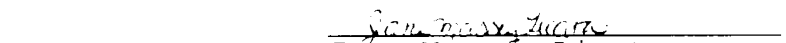
(XX) The Commissioner is hereby authorized to charge payment of the following fees during the pendency of this application or credit any overpayment to Deposit Account No. 12-1086. This sheet is attached in triplicate.

(XX) Any patent application processing fees under 37 CFR 1.17 and under 37 CFR 1.20(d).

( ) The issue fee set in 37 CFR 1.18 at or before mailing of the Notice of Allowance, pursuant to 37 CFR 1.311(b).

(XX) Any filing fees under 37 CFR 1.16 including fees for presentation of extra claims.

Respectfully submitted,



Jane Massey Licata
Registration No. 32,257

Date: **September 18, 1997**

Law Offices of
JANE MASSEY LICATA
66 E. Main Street
Marlton, New Jersey 08053

(609) 779-2400

RESPONSE UNDER 37 CFR 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP 1804

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No.:	PENN-0065
Inventors:	Wolfe and Fraser
Serial No.:	08/393,066
Filing Date:	February 23, 1995
Examiner:	D. Crouch
Group Art Unit:	1804
Title:	Method of Delivering Genes to the Central Nervous System of a Mammal

I, **Jane Massey Licata**, Registration No. **32,257**, certify that this correspondence is being deposited with the U.S. Postal Service as First Class mail in an envelope addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231.

On this date: **September 18, 1997**

Jane Massey Licata

Jane Massey Licata, Registration No. **32,257**

BOX AF
Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Dear Sir:

REPLY BRIEF

This reply brief is being filed in accordance with 37 C.F.R. §1.193(b) in response to the new ground of rejection raised in the Examiner's Answer dated July 25, 1997. The Examiner maintained the rejection of claims 1-9 under 35 U.S.C. §112, first paragraph, for lack of enablement. However, pending rejections under 35 U.S.C. §102 and 35 U.S.C. §103 were replaced by a new ground of rejection under 35 U.S.C. §103.

Specifically, claims 1-9 are now rejected under 35 U.S.C. §103 as being unpatentable over Dobson et al. (1989) *J. Virol.* 63, 3844-3851 in view of Nishimura et al. (1986) *Proc. Natl Acad. Sci.* 83, 7292-7296. Dobson et al. teach the delivery of rabbit β-globin gene to the peripheral nervous system of mice where expression of the gene is regulated by the HSV-1 latency promoter. As acknowledged by the Examiner, Dobson et al. do **not** teach delivery to the CNS nor delivery of β-glucuronidase operatively or tyrosine hydroxylase linked to promoter. However, the Examiner suggests that motivation to combine the teachings of Dobson et al. with Nishimura et al., teaching the DNA sequence for β-glucuronidase, is offered by Dobson et al. at page 3850, col 2, ¶ 3, lines 1-2 wherein it is taught that HSV-1 is a vector for the transfer of genes to neurons. The Examiner suggests that further motivation is found in Dobson et al. at page 3844, col 1, ¶ 1, lines 1-7, wherein it is taught that HSV can produce latent infections in both the PNS and the CNS and that the latency activated promoter, the LAT promoter, is active in such infections. Accordingly, the Examiner

suggests that given the teachings of Dobson et al. that an HSV-1 vector delivers genes of interest to the PNS and regulates expression of the gene from the LAT promoter, and that HSV inherently infects both the PNS and CNS, it would have been obvious to the ordinary skilled artisan at the time of filing to deliver any gene of interest to the CNS by administering the vector of Dobson et al.

Appellants respectfully disagree.

At the outset, it is pointed out that statements made at page 3850, col 2, ¶ 3, lines 1-2 are not that HSV-1 is a vector for the transfer of genes to neurons, but rather that "there is considerable interest in using HSV-1 as a vector for gene transfer to neurons." This statement could, at most, arguably provide a motivation to try to use an HSV-1 vector. However, the CAFC has consistently held that "obvious to try" is not to be equated with obviousness under 35 U.S.C. §103.

Further, teachings at page 3844, col 1, ¶ 1, lines 1-14 that HSV can produce latent infections in the CNS provide no reasonable expectation that HSV can be used as a vector to stably express a selected DNA sequence in the central nervous system by cells infected with the vector. As taught in the specification at page 2, to be useful a vector system must be capable of transferring a gene into the appropriate target cell which then stably expresses the transferred gene. However, latent viruses such as HSV are defined in the Dictionary of Biotechnology, as:

> a virus that remains within the host without producing any obvious effects. Activity may be induced, resulting in multiplication and the production of the disease symptoms long after the initial infection.

A copy of this definition is provided herewith as Appendix 1 for the Examiner's convenience. Accordingly, it is unpredictable based upon the teachings of the prior art whether a latent virus, such as HSV, which remains dormant in infected cells for long periods of time, could transfer a gene to cells of the CNS which then stably express that gene. As discussed at page 10 of the instant specification, the present invention provides the first demonstration that a foreign gene can be delivered to, and expressed over a long period of time (i.e., greater then 4 months) by neurons of the CNS by peripheral infection with a neurotropic virus. Thus, it is only with inappropriate hindsight that the Examiner could suggest that the combination of prior art provides the requisite motivation and reasonable expectation of success required to render the present invention obvious.

In an earnest effort to advance the prosecution of this case and in accordance with the Examiner's invitation to amend the claims in response to the new grounds of rejection, claims 1 and 8 have been amended to make clear that present invention provides a method of stably expressing a selected DNA in the CNS by infected cells, thus distinguishing the instant invention from any teachings of the prior art. Amended claims 1 and 8 are attached hereto as Appendix 2. As acknowledged by the Examiner at page 1 of the Office Action dated April 1, 1996, Appellants have shown that the

biologically active molecule, β-glucuronidase is expressed in the central nervous system when the DNA sequence encoding this molecule is operatively linked to the LAT promoter contained in the neurotropic virus, HSV. Accordingly, the amended claims introduce no new matter and are clearly enabled by teachings of the specification.

The amended claims not only distinguish the invention from the teachings of the prior art cited in the new rejection under 35 U.S.C. §103, but also meet the requirements of enablement set forth under 35 U.S.C. §112. Accordingly, these claims overcome all pending rejections. It is therefore respectfully requested that the amended claims set forth in Appendix 2 be entered and that the instant application be allowed.

Respectfully submitted,

Jane Massey Licata

Jane Massey Licata
Registration No. 32,257

Date: **September 18, 1997**

Law Offices of
JANE MASSEY LICATA
66 E. Main Street
Marlton, New Jersey 08053

(609) 779-2400